

Gonorrhea

Neisseria gonorrhoeae

Learning Objectives

Upon completion of this content, the learner will be able to

- Describe the epidemiology of gonorrhea in the U.S.
- Describe the pathogenesis of *Neisseria gonorrhoeae*.
- Discuss the clinical manifestations of gonorrhea.
- Identify common methods used in the diagnosis of gonorrhea.
- List CDC-recommended treatment regimens for gonorrhea.
- Summarize appropriate prevention counseling messages for patients with gonorrhea.
- Describe public health measures for the prevention of gonorrhea.

Lessons

- I. Epidemiology: Disease in the U.S.
- II. Pathogenesis
- III. Clinical manifestations
- IV. Diagnosis
- V. Patient management
- VI. Prevention

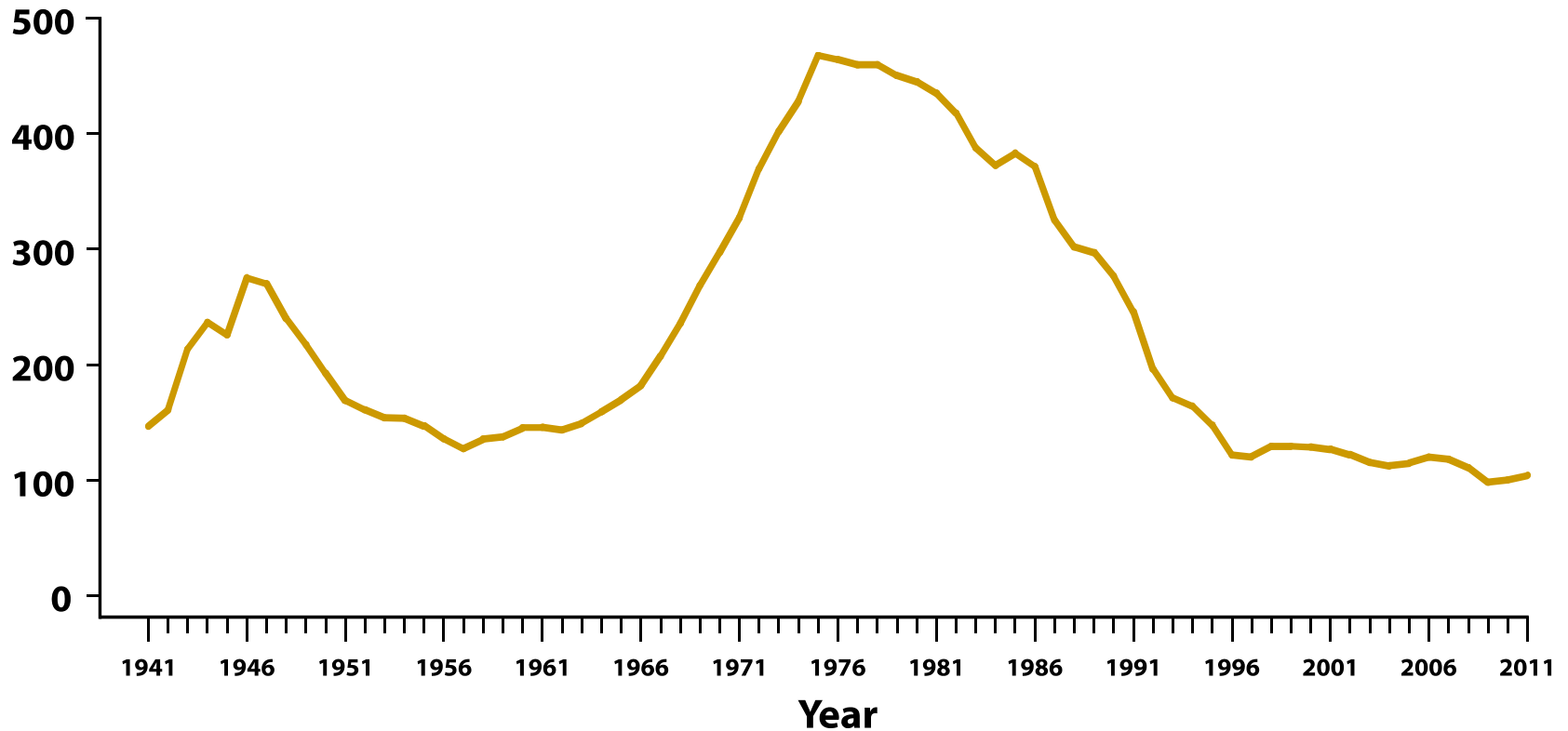
Lesson I: Epidemiology: Disease in the U.S.

Incidence and Prevalence

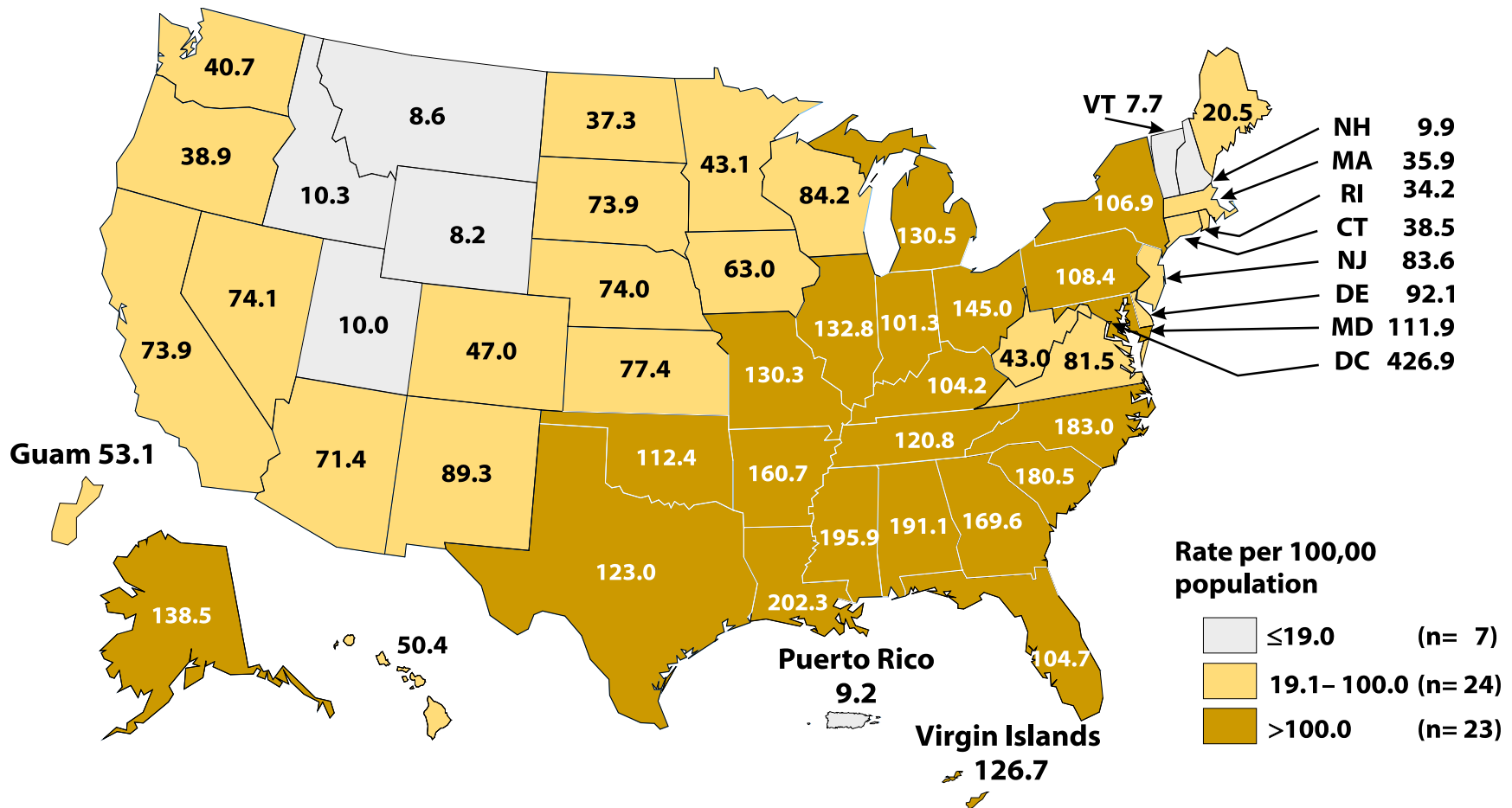
- Significant public health problem in U.S.
- Number of reported cases underestimates incidence
- Incidence remains high in some groups defined by geography, age, race/ethnicity, or sexual risk behavior
- Increasing proportion of gonococcal infections caused by resistant organisms

Gonorrhea—Rates, United States, 1941–2011

Rate (per 100,000 population)



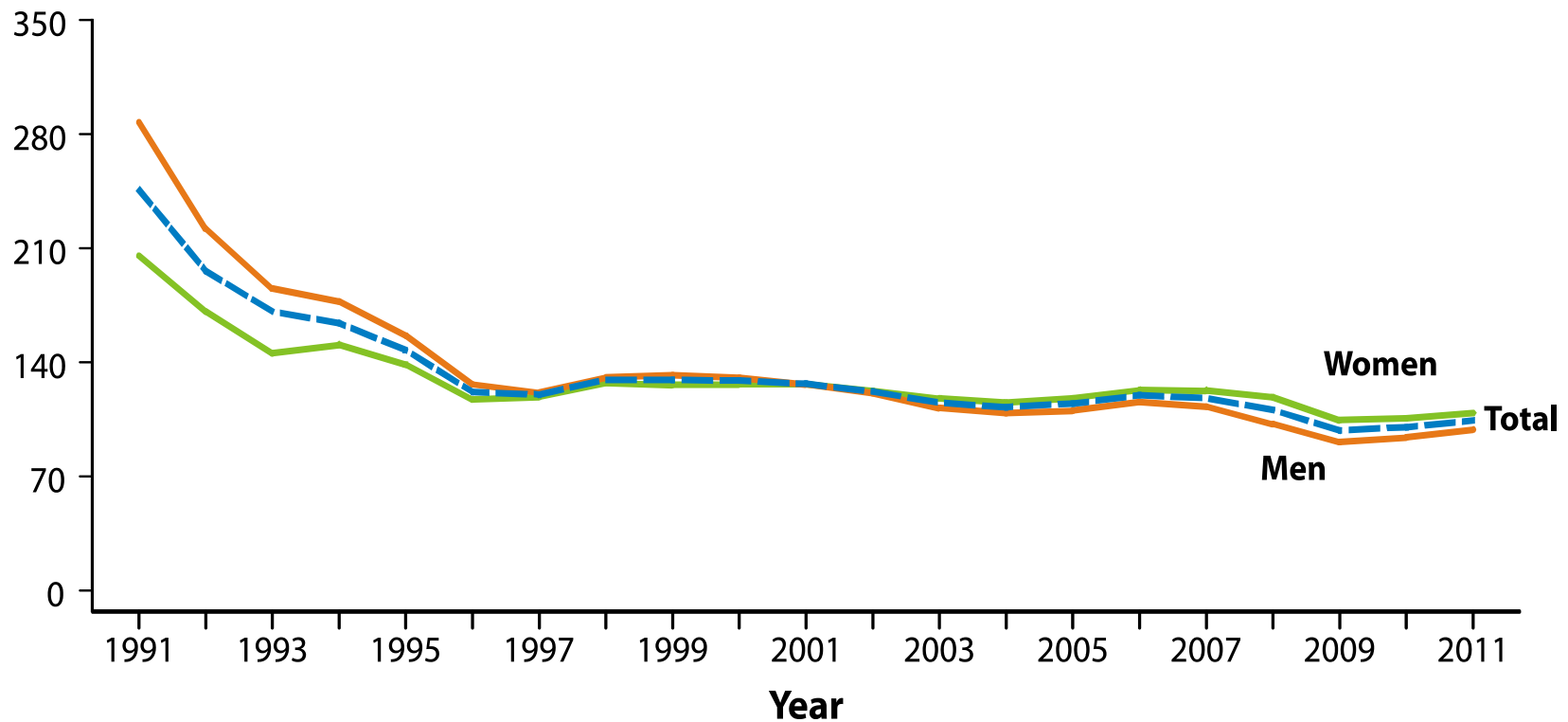
Gonorrhea—Rates by State, United States and Outlying Areas, 2011



NOTE: The total rate of gonorrhea for the United States and outlying area (Guam, Puerto Rico, and Virgin Islands) was 103.1 per 100,000 population. 7

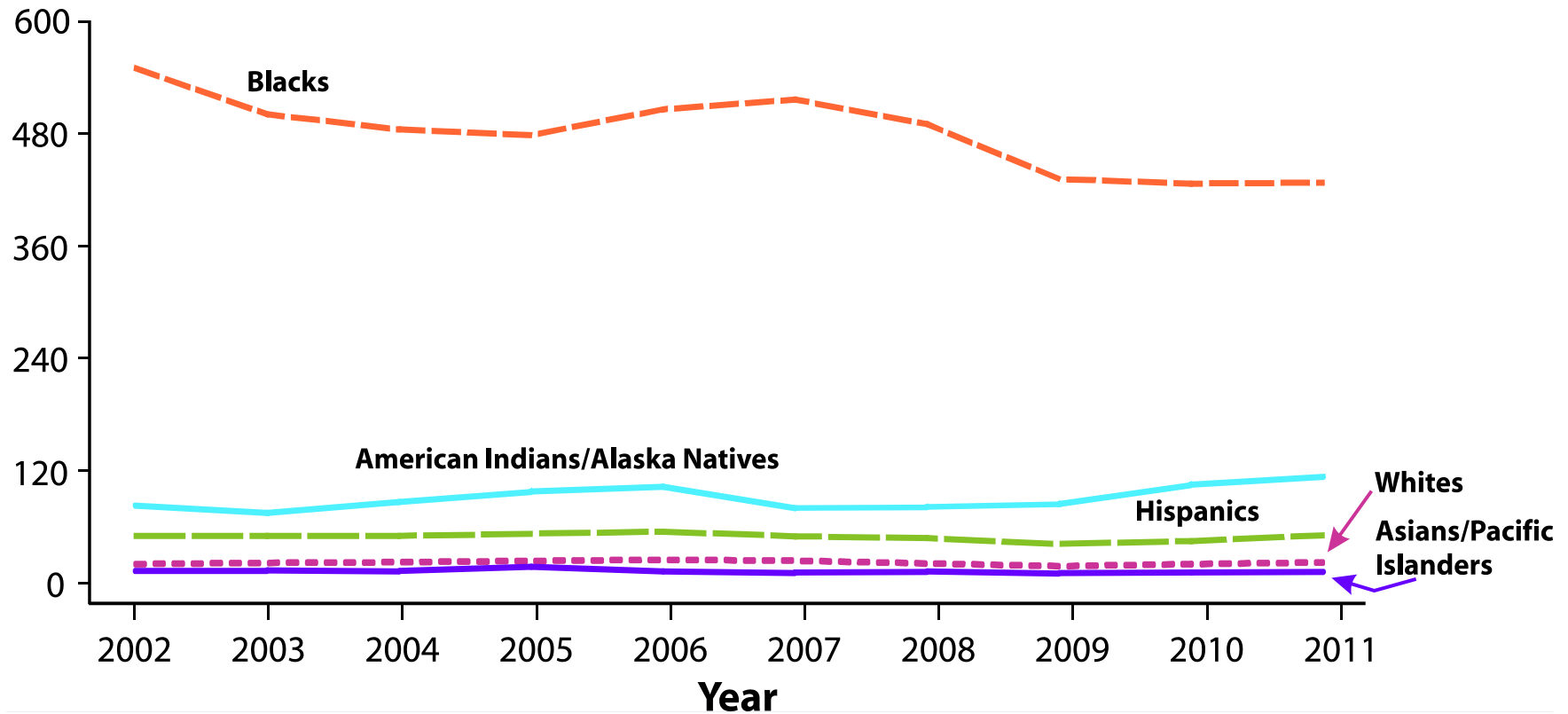
Gonorrhea—Rates by Sex, United States, 1991–2011

Rate (per 100,000 population)

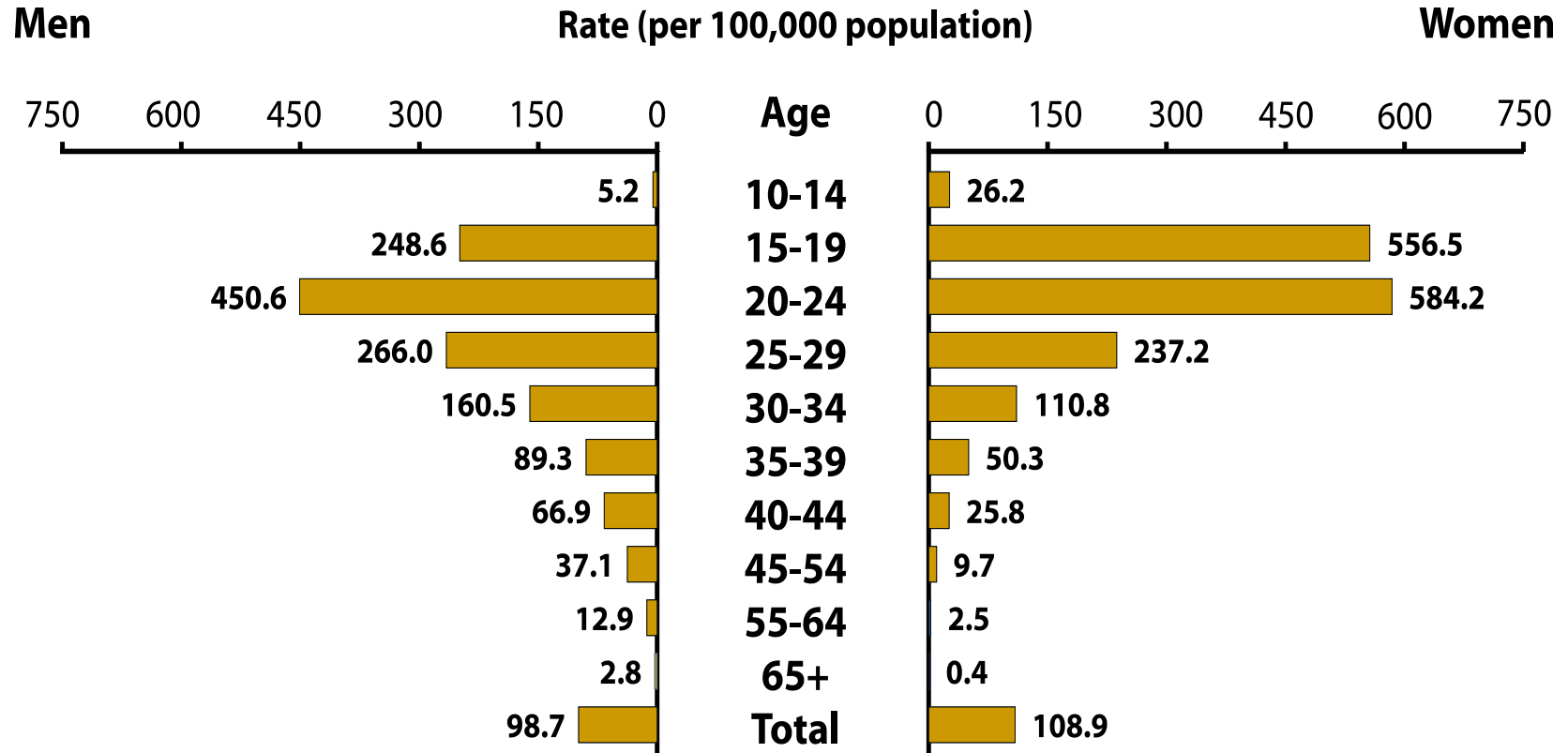


Gonorrhea—Rates by Race/Ethnicity, United States, 2002–2011

Rate (per 100,000 population)



Gonorrhea—Rates by Age and Sex, United States, 2011



Risk Factors

- Multiple or new sex partners or inconsistent condom use
- Urban residence in areas with disease prevalence
- Adolescent, females particularly
- Lower socio-economic status
- Use of drugs
- Exchange of sex for drugs or money
- African American

Transmission

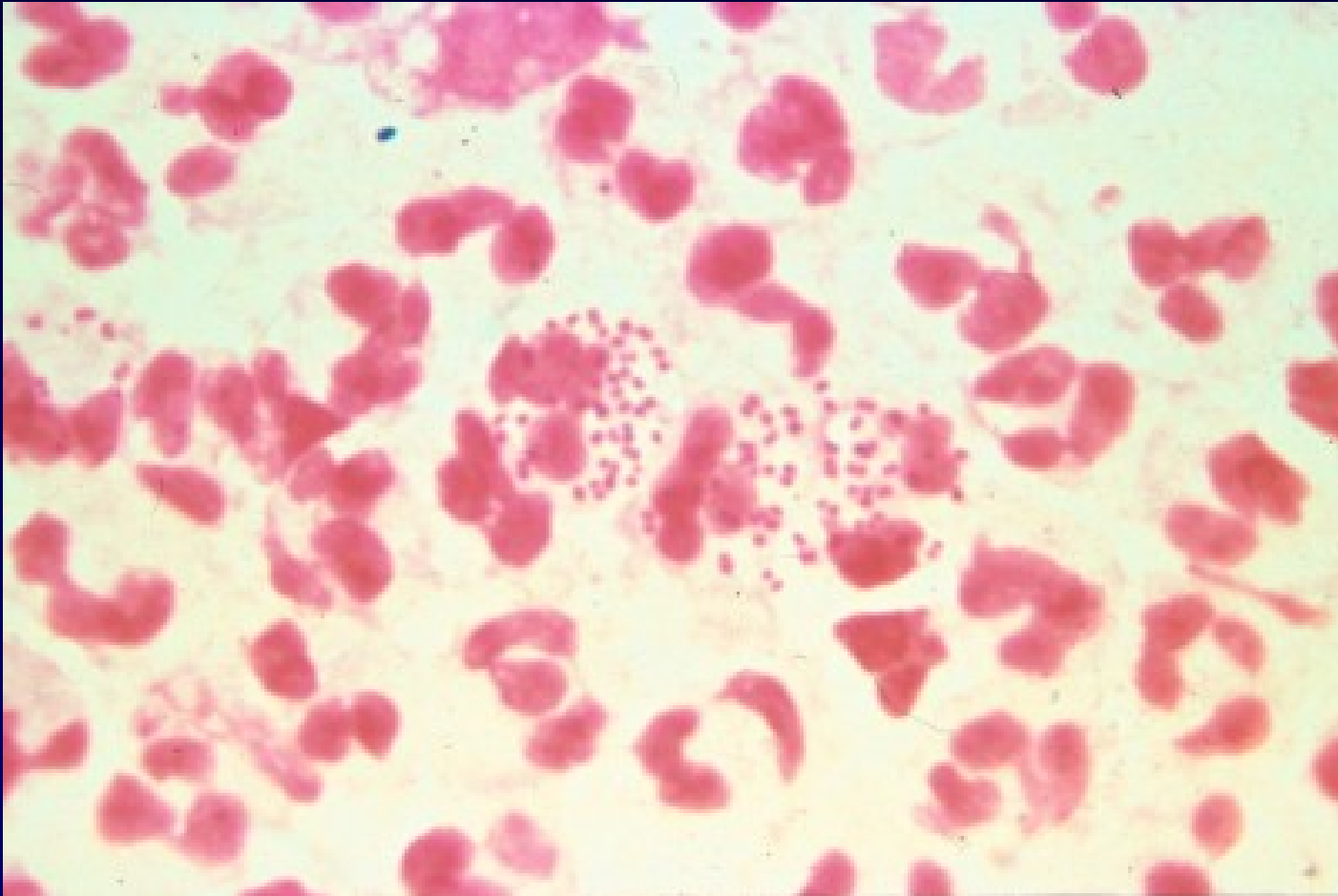
- Efficiently transmitted by
 - Male to female via semen
 - Vagina to male urethra
 - Rectal intercourse
 - Fellatio (pharyngeal infection)
 - Perinatal transmission (mother to infant)
- Gonorrhea associated with increased transmission of and susceptibility to HIV infection

Lesson II: Pathogenesis

Microbiology/Pathology

- Etiologic agent: *Neisseria gonorrhoeae*
- Gram-negative intracellular diplococcus
- Infects mucus-secreting epithelial cells
- Evades host response through alteration of surface structures

Gonorrhea: Gram Stain of Urethral Discharge



Lesson III: Clinical Manifestations

Genital Infection in Men

- Urethritis – Inflammation of urethra
- Epididymitis – Inflammation of the epididymis

Male Urethritis

- Symptoms
 - Typically purulent or mucopurulent urethral discharge
 - Often accompanied by dysuria
 - Discharge may be clear or cloudy
- Asymptomatic in a minority of cases
- Incubation period: usually 1-14 days for symptomatic disease, but may be longer

Gonococcal Urethritis: Purulent Discharge



Source: Seattle STD/HIV Prevention Training Center at the University of Washington:
Connie Celum and Walter Stamm

Epididymitis

- Symptoms: unilateral testicular pain and swelling
- Infrequent, but most common local complication in males
- Usually associated with overt or subclinical urethritis

Swollen or Tender Testicle (Epididymitis)



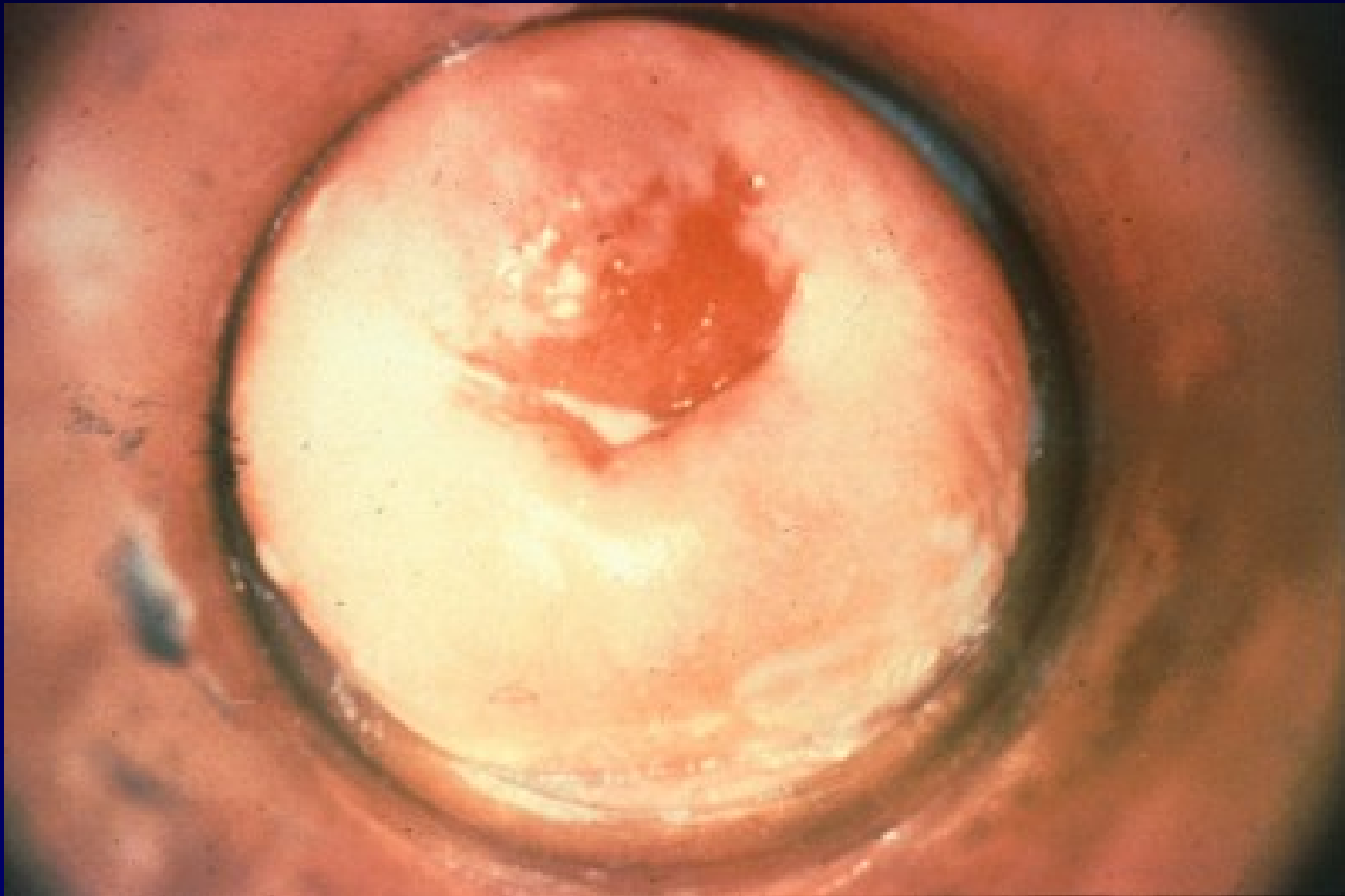
Genital Infection in Women

- Most infections are asymptomatic
- Cervicitis – inflammation of the cervix
- Urethritis – inflammation of the urethra

Cervicitis

- Non-specific symptoms: abnormal vaginal discharge, intermenstrual bleeding, dysuria, lower abdominal pain, or dyspareunia
- Clinical findings: mucopurulent or purulent cervical discharge, easily induced cervical bleeding
- At least 50% of women with clinical cervicitis have no symptoms
- Incubation period unclear, but symptoms may occur within 10 days of infection

Gonococcal Cervicitis



Urethritis

- Symptoms: dysuria, however, most women are asymptomatic
- 70%–90% of women with cervical gonococcal infection may have urethral infection

Complications in Women

- Accessory gland infection
 - Bartholin's glands
 - Skene's glands
- Pelvic Inflammatory Disease (PID)
 - May be asymptomatic
 - May present with lower abdominal pain, discharge, dyspareunia, irregular menstrual bleeding and fever
- Fitz-Hugh-Curtis Syndrome
 - Perihepatitis

Bartholin's Abscess



Syndromes in Men and Women

- **Anorectal infection**

- Usually acquired by anal intercourse
- Usually asymptomatic
- Symptoms: anal irritation, painful defecation, constipation, scant rectal bleeding, painless mucopurulent discharge, tenesmus, and anal pruritus
- Evaluate utilizing an anoscopic examination
- Signs: mucosa may appear normal, or purulent discharge, erythema, or easily induced bleeding may be observed with anoscopic exam

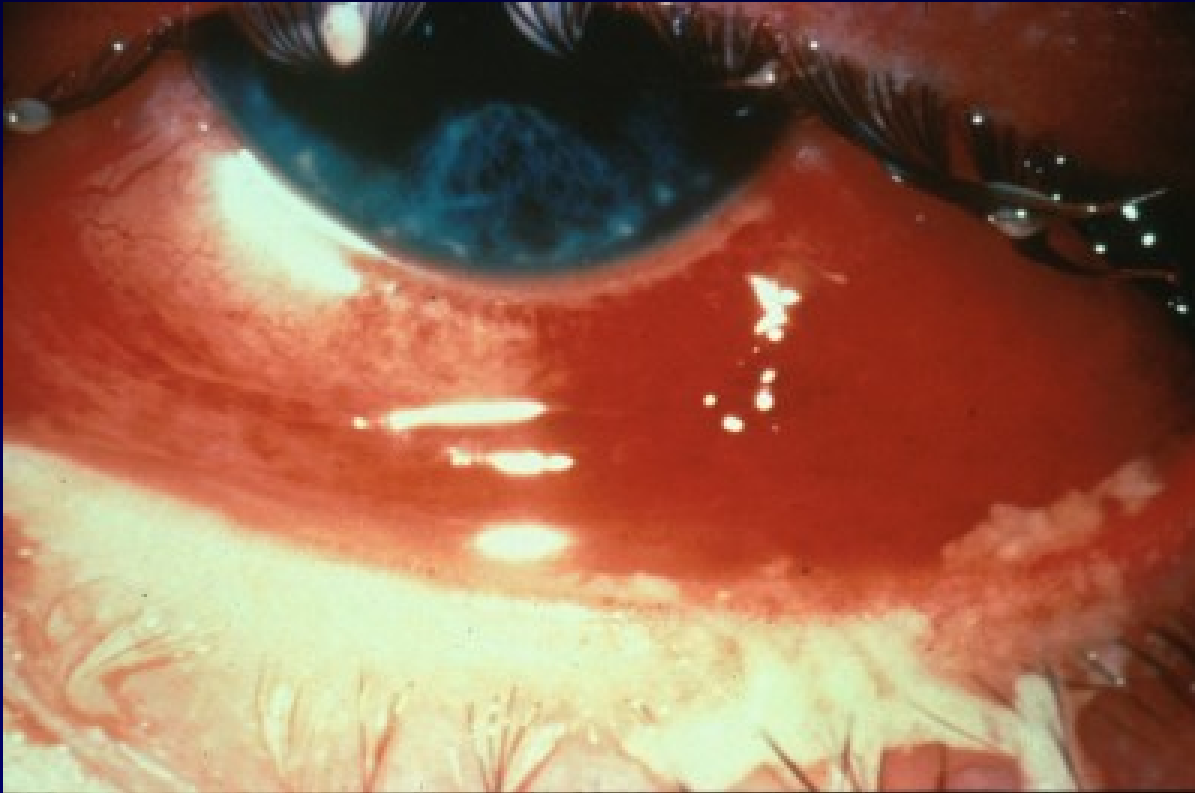
- **Pharyngeal infection**

- May be sole site of infection if oral-genital contact is the only exposure
- Most often asymptomatic, but symptoms, if present, may include pharyngitis, tonsillitis, fever, and cervical adenitis

Syndromes in Men and Women (continued)

- **Conjunctivitis**
 - Usually a result of autoinoculation in adults
 - Symptoms/signs: eye irritation with purulent conjunctival exudate
- **Disseminated gonococcal infection (DGI)**
 - Systemic gonococcal infection
 - Occurs infrequently. More common in women than in men
 - Associated with a gonococcal strain that produces bacteremia without associated urogenital symptoms
 - Clinical manifestations: skin lesions, arthralgias, tenosynovitis, arthritis, hepatitis, myocarditis, endocarditis, and meningitis

Gonococcal Ophthalmia



Disseminated Gonorrhea— Skin Lesion on Foot



Gonococcal Infection in Children

- Perinatal: infections of the conjunctiva, pharynx, respiratory tract or anal canal
- Older children (>1 year): considered possible evidence of sexual abuse
- Vulvovaginitis, not cervicitis, in prepubescent girls
- Anorectum or pharynx more commonly infected in boys than urethra
- Because of legal implications, culture remains the preferred method of diagnosis

Lesson IV: Diagnosis

Diagnostic Methods

- Culture tests
 - Advantages: low cost, suitable for a variety of specimen sites, antimicrobial susceptibility can be performed
 - Anatomic sites to test: in response to exposure history in persons at significant risk of gonococcal infection, complaints, or clinical findings
 - In men: urethra in all men; pharynx and rectum, depending on exposure history or symptoms
 - In women: cervix should be tested; pharynx and rectum depending on symptoms and exposure history; vagina may be tested if cervix is absent; Bartholin's or Skene's glands may be cultured if overt exudate is expressed

Diagnostic Methods (continued)

- Non-culture tests
 - Amplified tests (NAATs)
 - Polymerase chain reaction (PCR) (Roche Amplicor)
 - Transcription-mediated amplification (TMA) (Gen-Probe Aptima)
 - Strand displacement amplification (SDA) (Becton-Dickinson BD ProbeTec ET)
 - Non-amplified tests
 - DNA probe (Gen-Probe PACE 2, Digene Hybrid Capture II)
 - Gram-stained smear

Clinical Considerations

- In cases of suspected sexual abuse
 - Adults
 - NAATs are preferred for diagnostic evaluation of sexual assault regardless of penetration
 - Children
 - Culture remains the preferred method for urethral specimens or urine from boys and for extragenital specimens for all children
 - NAATs can be used as an alternative to culture with vaginal specimens or urine from girls

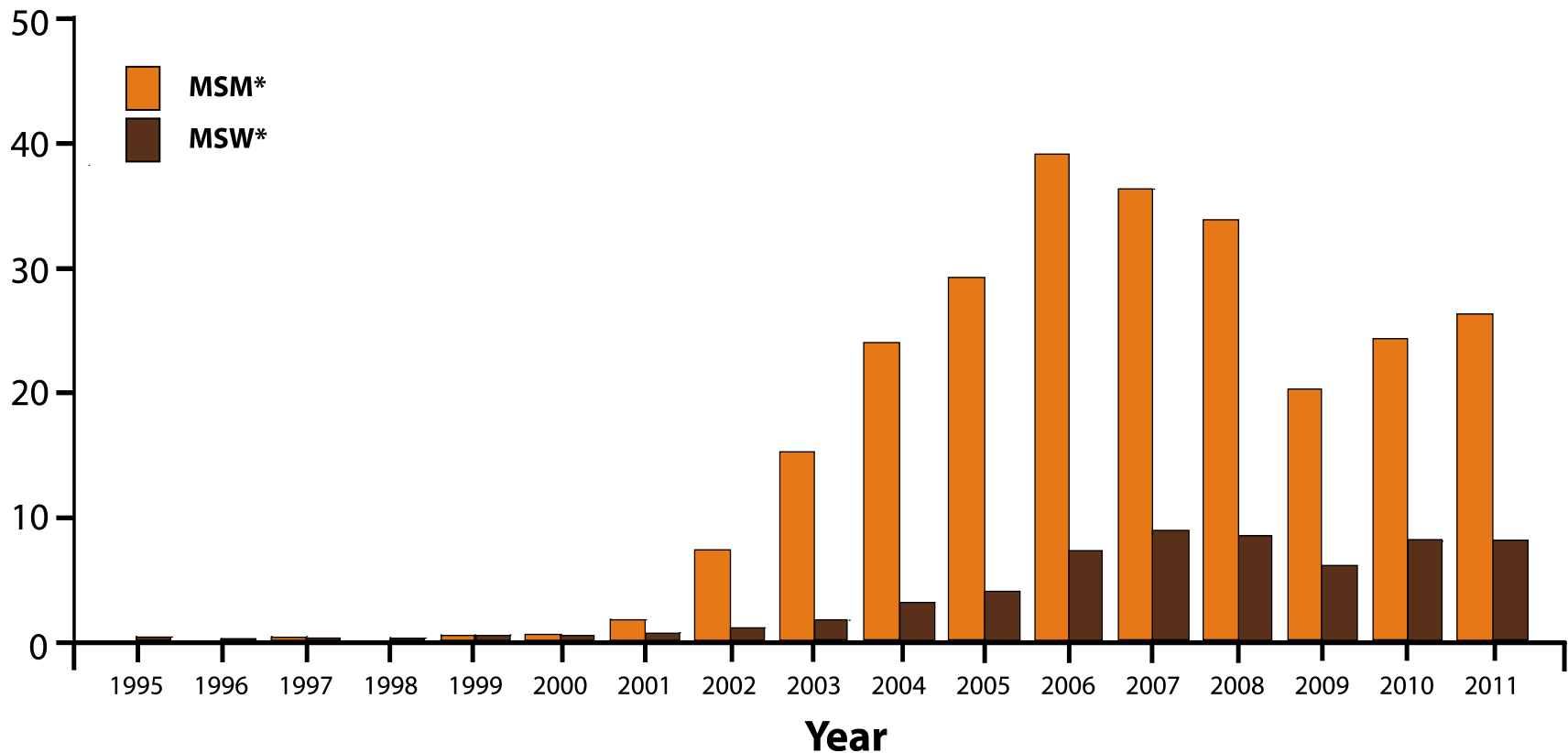
Lesson V: Patient Management

Antimicrobial Susceptibility of *N. gonorrhoeae*

- Fluoroquinolone resistance is widely disseminated throughout the U.S. and the world
- Approximately 25% of isolates are resistance to penicillin or tetracycline or both
- In 2011, 0.3% of isolates showed decreased susceptibility to azithromycin, down from 0.5% in 2010.
- Sporadic cases of decreased susceptibility to ceftriaxone and cefixime have been reported recently

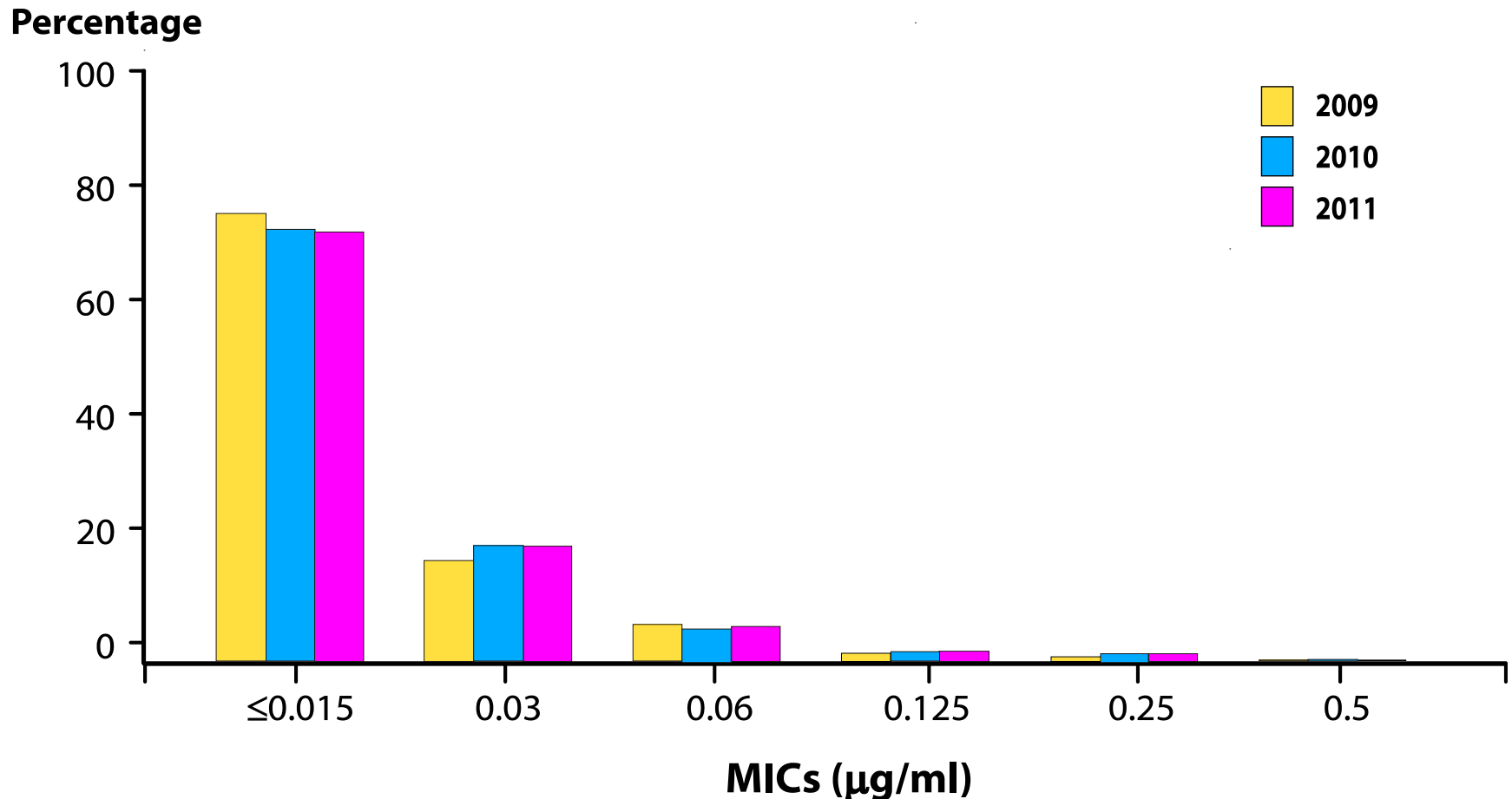
Percentage of *Neisseria gonorrhoeae* Isolates that are Ciprofloxacin-Resistant by Sex of Sex Partner, Gonococcal Isolate Surveillance Project (GISP), 1995–2011

Percentage



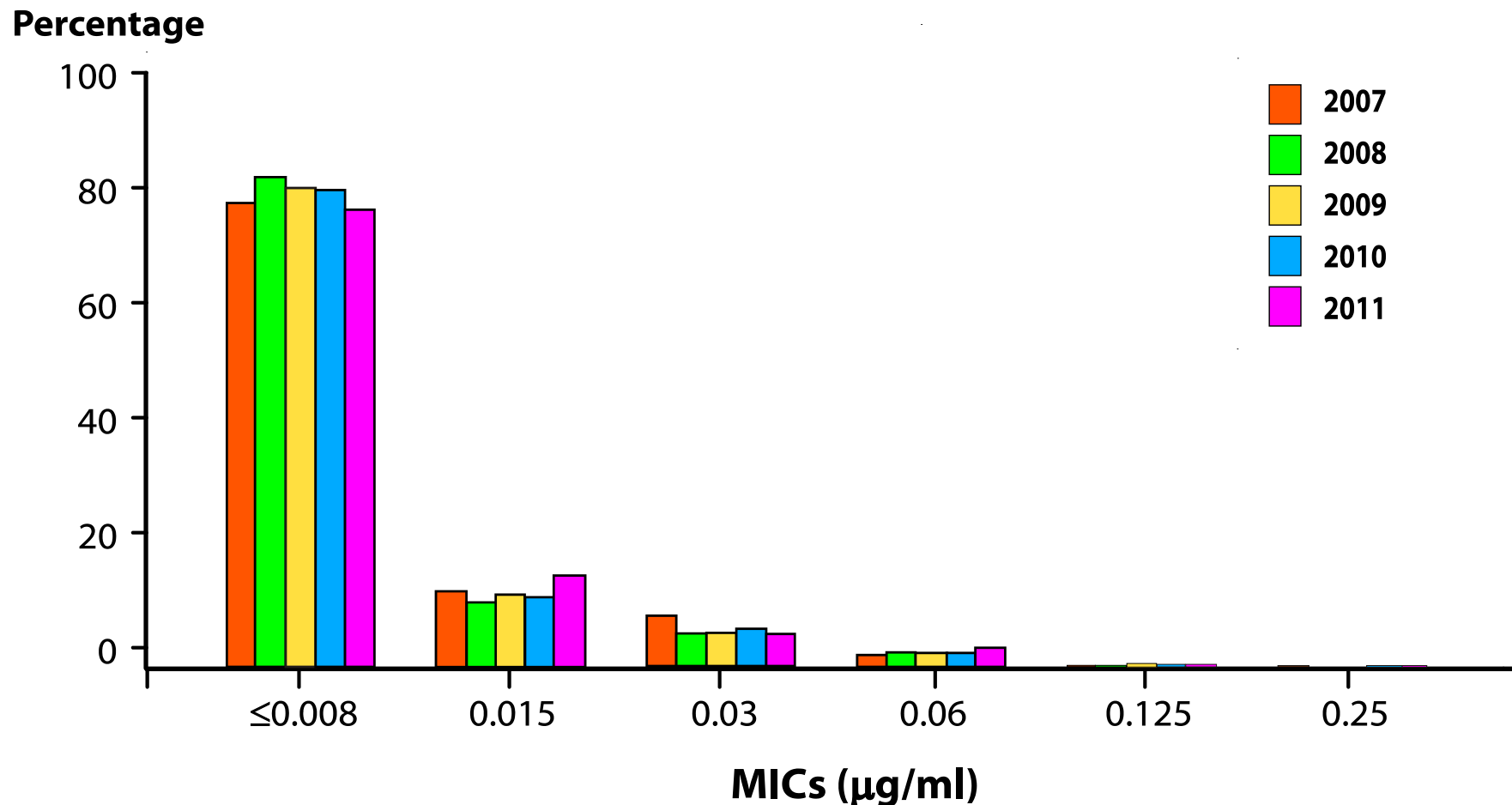
*MSM=men who have sex with men; MSW=men who have sex with women only.

Distribution of Minimum Inhibitory Concentrations (MICs) of Cefixime Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2009–2011



- NOTE:** Isolates were not tested for cefixime susceptibility in 2007 and 2008

Distribution of Minimum Inhibitory Concentrations (MICs) of Ceftriaxone Among *Neisseria gonorrhoeae* Isolates, Gonococcal Isolate Surveillance Project (GISP), 2007–2011



Treatment for Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Recommended

Ceftriaxone	250 mg	IM	Once
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PLUS

Azithromycin	1 g	Orally	Once
OR			
Doxycycline	100 mg	Orally	Twice a day for 7 days

Quinolones are no longer recommended in the United States for the treatment of gonorrhea and associated conditions, such as PID

Treatment for Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Alternative 1: *If Ceftriaxone is not available*

Cefixime	400 mg	Orally	Once
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PLUS

Azithromycin	1 g	Orally	Once
OR			
Doxycycline	100 mg	Orally	Twice a day for 7 days

PLUS

Test of cure in 1 week

Treatment for Uncomplicated Gonococcal Infections of the Cervix, Urethra, and Rectum

Alternative 2: *If patient is cephalosporin-allergic*

Azithromycin	2 g	Orally	Once
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PLUS

Test of cure in 1 week

Treatment for Uncomplicated Gonococcal Infections of the Pharynx

Ceftriaxone	250 mg	IM	Once
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PLUS

Azithromycin	1 g	Orally	Once OR
Doxycycline	100 mg	Orally	Twice a day for 7 days

Special Considerations: Pregnancy

- Treat with recommended cephalosporin-based combination therapy
- If cephalosporin is not tolerated, treat with azithromycin 2 g orally. A test of cure should be performed 1 week after treatment
- Pregnant women should not be treated with quinolones or tetracyclines. Spectinomycin is not commercially available

Penicillin-Allergic

- Azithromycin 2 g orally
 - Plus test of cure in 1 week
- Desensitization is impractical in most settings

Follow-Up

- A test of cure is not recommended if recommended regimen is administered
- A test of cure is recommended if an alternative regimen is administered
- If symptoms persist, perform culture for *N. gonorrhoeae*
 - Any gonococci isolated should be tested for antimicrobial susceptibility at site of exposure
- Repeat testing in 3 months

Lesson VI: Prevention

Screening

- **Pregnancy:**
 - A test for *N. gonorrhoeae* should be performed at the 1st prenatal visit for women at risk or those living in an area in which the prevalence of *N. gonorrhoeae* is high
 - Repeat test in the 3rd trimester for those at continued risk
- **U.S. Preventive Service Task Force** recommends screening all sexually active women for gonorrhea infection if they are at increased risk of infection
- **Sexually active men who have sex with men:** CDC recommends screening at least annually at all anatomic sites of exposure

Partner Management

- Evaluate and treat all sex partners for *N. gonorrhoeae* and *C. trachomatis* infections, if contact was within 60 days of symptoms or diagnosis
- If a patient's last sexual intercourse was >60 days before onset of symptoms or diagnosis, the patient's most recent sex partner should be treated
- Avoid sexual intercourse until therapy is completed and both partners no longer have symptoms

Reporting

- Laws and regulations in all states require that persons diagnosed with gonorrhea are reported to public health authorities by clinicians, labs, or both

Patient Counseling/Education

- Nature of disease
 - Usually symptomatic in males and asymptomatic in females
 - Untreated infections can result in PID, infertility, and ectopic pregnancy in women and epididymitis in men
- Transmission issues
 - Efficiently transmitted
- Risk reduction
 - Utilize prevention strategies

Case Study



History: Robert Forbes

- 33-year-old male who presents to his doctor reporting a purulent urethral discharge and dysuria for 3 days.
- Lives in Dallas with history of travel to Las Vegas 3 weeks ago.
- New female sex partner (Laura) for 2 months. They have unprotected vaginal intercourse 4 times/week, the last time being 2 days ago. No oral or rectal sex.
- Also had a one-time sexual encounter with a woman he met in Las Vegas 3 weeks ago (Monica). They had oral and vaginal sex. No condoms used.
- No history of urethral discharge or STDs, no sore throat or rectal discomfort. Negative HIV test 1 year ago.

Physical Exam

- Vital signs: blood pressure 98/72, pulse 68, respiration 14, temperature 37.2° C
- Cooperative, good historian
- Chest, heart, musculoskeletal, and abdominal exams within normal limits
- No flank pain on percussion, normal rectal exam, no sores or rashes
- The genital exam reveals a reddened urethral meatus with a purulent discharge, without lesions or lymphadenopathy

Questions

1. What should be included in the differential diagnosis?
2. Which laboratory tests are appropriate to order or perform?
3. What is the appropriate treatment regimen?

Laboratory Results

Results of laboratory tests:

- Urethral and pharyngeal culture: showed growth of a Gram-negative diplococcus that was oxidase-positive. Biochemical and FA conjugate testing confirmed this isolate to be *N. gonorrhoeae*.
 - NAAT for chlamydia: negative
 - RPR: nonreactive
 - HIV antibody test: negative
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- 4) What is the diagnosis, based on all available information?
 - 5) Who is responsible for reporting this case to the local health department?



Partner Management



Robert's sex partners within the past 3 months:

- Laura: Last exposure - Unprotected vaginal sex 2 days ago
- Monica: Last exposure - Unprotected oral (Monica performed fellatio) and vaginal sex 3 weeks ago while he was in Las Vegas
- Jerilyn: Last exposure - Unprotected vaginal sex 3 months ago



- 6) Laura was examined and her lab results came back negative for gonorrhea and chlamydia. How should Laura be managed?
- 7) What tests should Jerilyn and Monica have?

Follow-Up

Robert returns 4 months later for an employer-sponsored flu shot. He took his medications as directed, is asymptomatic, and has had no sex partners since his office visit to you.

8) Does Robert need repeat testing for gonorrhea?

9) What are appropriate prevention counseling messages for Robert?